Surgical Outcomes of Endoscopic Endonasal Surgery in 29 Patients with Craniopharyngioma

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Abstract

Background Recently the endoscopic endonasal surgery (EES) has been introduced as a modality for the treatment of patients with craniopharyngiomas. In this study, we describe our initial experience in treatment of 29 patients with craniopharyngiomas using this approach.

Methods Twenty-nine consecutive patients with craniopharyngiomas who had undergone EES in a 5-year period were studied retrospectively. Patients underwent preoperative and postoperative endocrinologic and ophthalmologic evaluations. Radiologic characteristics of tumors and extent of resection were determined. The recurrence and complications were evaluated.

Results Pituitary and visual dysfunction were observed preoperatively in 89.7 and 86% of patients, respectively. After EES, visual outcome either showed an improvement or else remained unchanged in 92.3% of the cases; however, pituitary function remained unchanged and even got worsened in 34.6% of the cases. Prevalence of diabetes insipidus before and after surgery was 58.6 and 69.2%. The rate of gross total resection was 62%. Moreover, 86.2% of the tumors were almost totally resected (more than 95% of the tumor size resected). After surgery, cerebrospinal fluid (CSF) leak and meningitis occurred in four (13.8%) and two (6.9%) patients, respectively. Perioperative mortality was seen in two of the cases (6.9%). The mean follow-up was 25 months and tumor recurrence was discovered in four patients (15.3%).

Conclusion The EES with the goal of maximal and safe tumor resection could be used for the treatment of most craniopharyngiomas. Although the rates of visual improvement and gross tumor resection are high, CSF leak, pituitary dysfunction, and meningitis are serious concerns.

Keywords
- endoscopic endonasal surgery
- craniopharyngioma
- outcome
- complication

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Introduction

Craniopharyngioma is known as benign and a rare tumor which originates from the coatings of the Rathke's pouch. According to the WHO, craniopharyngioma is classified as a grade I tumor regarding its histological properties. The tumor has a similar incidence rate between both sexes; however, the incidence peaks at the age periods of 5 to 15 years and 50 to 74 years.[1,2]

Despite the benign histology, there are no definite treatments for this tumor, and its adhesion to the stalk of the pituitary gland, optic chiasma, hypothalamus, or even cerebral vessels, makes complete resection unattainable. So, craniopharyngioma is considered as a "benign tumor in a malignant location."[3]

Currently, surgical resection with or without adjuvant radiotherapy is performed as the primary treatment for patients affected with these tumors. The applied approach is chosen based on anatomical characteristics of the tumor, patient's age, and associated illnesses. In this regard, different surgical modalities can be applied. These modalities include transcranial approach with craniotomy, endoscopic endonasal approach, cyst aspiration, or stereotactic biopsy.[4,5]

Endoscopic endonasal surgery (EES) has recently been introduced as a potential surgical option for the resection of craniopharyngiomas. This technique allows a safe and direct access to the tumor site and has been shown to be associated with significantly lower incidence of complications where vital structures such as hypothalamus, optic nerves and chiasma, carotid and basilar arteries, circle of Willis, and its associated branches or the pituitary stalk are involved.[6,7]

Given the development and increasing use of endoscopic techniques, the EES seems to be replacing the classic transcranial approaches. However, considering the low incidence of craniopharyngiomas, further studies are needed to validate this approach. In this regard, the current study investigates the results of EES in patients with craniopharyngiomas, radiological characteristics, and further evaluates patients' clinical manifestations and short-term outcome.

Methods

Study Population

Ethics Committee of Tehran University of Medical Sciences approved this study (IRB Code: 9211255006), and all applied methods were according to the Helsinki declaration. Twenty-nine patients with craniopharyngiomas operated with EES technique at Imam Khomeini Hospital in Tehran, from May 2013 to March 2018, were evaluated. Demographic data and clinical manifestations were collected by a series of questionnaires, interview, and review of medical records of patients.

Preoperative Data

All of the included patients were routinely examined for visual acuity and visual field at the same institute. In addition, complete profile of pituitary hormones was examined. Furthermore, all patients had undergone neuroradiological evaluations including brain magnetic resonance imaging (MRI) with and without intravenous gadolinium injection and brain computed tomography scan with and without intravenous contrast agent (with neuronavigation protocol). Tumor volume was assessed by a modified ellipsoid volume, that is, $(A \times B \times C)/2$, where A, B, and C are the maximum diameters of the tumor in each of the three dimensions.[8] Puget classification was also used for the evaluation of the degree of hypothalamic involvement.[9] In this classification, three grades are introduced based on preoperative MRI: Grade 0: There is no involvement of the hypothalamus; Grade I: The tumor causes displacement of the hypothalamus or has a compressive effect on I; Grade II: the hypothalamus has severe involvement and is not detectable in MRI.

Operation Technique

The endoscopic endonasal transsphenoidal approach under neuronavigation guide (PARSIS: Parseh Intelligent Surgical System Co., IRI) was used for surgery. A dedicated team of surgeons was the same for all patients and consisted of a neurosurgeon and an ENT surgeon. The tumor resection rate was determined based on intraoperative evaluation as well as postoperative MRI. In most patients, the extended type of this approach was used and following the extensive sphenoidectomy, planum and tuberculum sella were drilled. After the tumor's decompression, the tumor's capsule was dissected and detached from the pituitary stalk, optic nerves and chiasm, and vascular system. For dural reconstruction, an onlay fat layer and fasciae lata were used. At the end, for reinforcement, a nasoseptal flap prepared at the beginning of surgery was placed on fasciae lata. More details of the surgical procedure have been provided in previous studies.[9–11]

Post Surgery

The results of surgery were evaluated by clinical examination, visual, and endocrinologic tests, and brain MRI during the 3 three months after surgery and then every 6 months if applicable.

During the first 48 hours after surgery, brain MRI was performed in all patients to have a baseline imaging for postoperative follow-ups. The tumor resection rate was determined by comparing the primary post-surgery tumor volume with the preoperative results. Extent of resection on postoperative MRI was defined as gross total resection (GTR), near total resection (NTR) subtotal resection (STR), and partial tumor resection in which more than 95% and less than 95 and 80% of the tumor was removed, respectively. Recurrence and progression were defined as the appearance of new tumor after a previous GTR or the growth of residual tumor after NTR or STR.

Statistical Analysis

The obtained data were analyzed by IBM SPSS, Version 24.0 (IBM Corp. Released 2013. Armonk, New York, United States). Based on its type, data were described as mean and standard deviation, frequency, or percentage. To compare the discrete variables, Chi-square or Fisher's exact test were used, and for comparing continuous variables, the Student's *t*-test and

Table 1 Demographic characteristics and clinical symptoms of 29 patients with craniopharyngioma

Characteristics	Type	Previous treatment status		Total	*p*-Value
		Primary	Secondary		
No. of patients		18	11	29	
Age	Median (y)	30.83	29.36	30.28	0.797
	Range	2.5–52	8–48	2.5–52	
Gender	Male	11 (61.1%)	6 (54.5%)	17 (58.6%)	0.999
	Female	7 (39.9%)	5 (45.5%)	12 (41.4%)	
Maturity	Adult	13 (72.2%)	8 (72.7	21 (72.5%)	0.999
	Child	5 (27.8%)	3 (27.3%)	8 (27.5%)	
Visual impairment		15 (83.3%)	10 (90.90%)	25 (86.2%)	0.999
Headache		13 (76.5%)	4 (36.4%)	17 (60.7%)	0.053
Ant. pituitary function	Normal	3 (16.7%)	0 (0.0%)	3 (10.3%)	0.151
	Partial dysfunction	10 (55.6%)	4 (36.4%)	14 (48.3%)	
	Panhypopituitarism	5 (27.8%)	7 (63.6%)	12 (41.4%)	
DI		9 (50.0%)	8 (72.7%)	17 (58.6%)	0.273
CNS palsy		4 (22.2%)	2 (18.2%)	6 (20.7%)	0.999

Abbreviations: CNS, central nervous system; DI, diabetes insipidus.

ANOVA were employed. A *p*-value less than 0.05 was considered statistically significant.

Results

Patients' Characteristics

Among the 29 included patients with craniopharyngioma, there were 21 adults and eight children defined as being under 18 years of age. The mean age of the patients was 30.28 years (Age range: 8–52 years) with the standard deviation of 15.04 years. Eighteen (62%) tumors were primary; while, eleven patients (38%) had recurrent or residual tumors (secondary tumors).

Visual impairment as the most common symptom was seen in 44.8% of the cases (13 patients). This was followed by headache in seven patients (24.1%) and delayed puberty in three patients (10.3%) as the next ranks. Out of the remaining six patients, two children had been referred due to growth retardation while two adults had mental status changes, a patient had experienced seizure, and another one had hemiparesis. Demographic characteristics and clinical symptoms of the patients are depicted in ►**Table 1**. As it is shown, there was no significant difference between patients with primary and secondary (recurrent/residual) tumors (p-value > 0.05).

The mean tumor volume in all patients was 24.07 cm^3 (6–69 cm^3), and the maximum tumor diameter varied from 20 to 61 mm with an average of 39.90 mm. ►**Table 2** presents the radiological characteristics of tumors including the existence of cysts, extension to the third ventricle or interpeduncular cistern, and also patient's preoperative Puget classification is shown in ►**Table 2**.

The tumor size can be divided into four groups of small (less than 2 cm), medium (2–4 cm), large (4–6 cm), and giant (more than 6 cm) tumor size. In our study, only two tumors were categorized in the giant group, and most of them (89%) had a medium to large size (►**Table 2**). Eight patients (27.6%) had hydrocephalus-related findings in preoperative imaging. Two of them had undergone ventriculoperitoneal shunt previously. In one of the patients emergent external ventricular drainage (EVD) was performed, but the subject expired because of evolving ventriculitis. In five patients, hydrocephalus got resolved in postoperation imaging studies.

According to Puget classification, four patients (13.8%) were categorized in grade 0, 12 (41.4%) in grade I, and 13 (44.8%) in grade II.

Operation

All 29 patients underwent EES. The goal was GTR for every case; however, this was not possible in some patients due to the adhesion and extension of the tumor to vital neurovascular elements.

Extended endoscopic endonasal approach (transtuberculum/transplanum) was applied in 17 (58.6%); while due to the small tumor size or enlargement of the sella, transsellar corridor was found to be sufficient for tumor resection in other cases (12 cases, 41.4%).

GTR was only performed in 18 (62%) patients (►**Fig. 1**). Seven cases (24.1%) underwent NTR (>95%) for safe resection. Only four patients had resections less than 95% (►**Fig. 2**). According to the statistical analysis, irrespective of being a primary or secondary tumor, tumor size (less than or greater than 5 cm) and Puget grade made no significant difference in resection rate (p-value >0.05; ►**Table 3**).

Post-Surgical Evaluations

According to the outpatient evaluation and follow-up, the visual function was improved in 18 patients (72%) from the 25 cases with preoperative visual impairment; it was unchanged and

Table 2 Radiological findings of craniopharyngioma tumors

Radiologic finding		No (%)		Total	*p*-Value
		Primary	Secondary		
No. of patients		18	11	29	
Mean tumor volume (cm^3)		26.11	20.73	24.07	0.486
Mean maximum diameter (mm)		41.72	36.91	39.90	0.310
Range of max. diameter	<20 mm	0 (0.0%)	1 (9.1%)	1 (3.4%)	0.652
	21–40 mm	9 (50.0%)	5 (45.5%)	14 (48.3%)	
	>40 mm	9 (50.0%)	5 (45.5%)	14 (48.3%)	
Max. diameter >50 mm		6 (33.3%)	2 (18.2%)	8 (27.6%)	0.671
Tumor location	Sellar	2 (11.1%)	1 (9.1%)	3 (10.3%)	0.999
	Suprasellar	1 (5.6%)	0 (0.0%)	1 (3.4%)	
	Sellar/suprasellar	15 (83.3%)	10 (90.9%)	25 (86.2%)	
Tumor consistency	Solid	1 (5.6%)	2 (18.2%)	3 (10.3%)	0.185
	Cystic	4 (22.2%)	0 (0.0%)	4 (13.8%)	
	Mixed	13 (72.2%)	9 (81.8%)	22 (75.9%)	
Contrast enhancement	Heterogenous	12 (66.7%)	9 (81.8%)	21 (72.4%)	0.444
	Homogenous	1 (5.6%)	1 (9.1%)	2 (6.9%)	
	Ring enhancement	5 (27.8%)	1 (9.1%)	6 (20.7%)	
Calcification		14 (77.8%)	9 (81.8%)	23 (79.3%)	0.999
Hydrocephalus		5 (27.8%)	3 (27.3%)	8 (27.6%)	0.999
Relation to third ventricle	None	2 (11.1%)	3 (27.3%)	5 (17.2%)	0.353
	Floor compression	5 (27.8%)	4 (36.4%)	9 (31.0%)	
	Intraventricular extension	11 (61.1%)	4 (36.4%)	15 (51.7%)	
Interpeduncular cistern involvement		13 (72.2%)	7 (63.6%)	20 (69.0%)	0.694
Preop. Puget classification	Grade 0	2 (11.1%)	2 (18.2%)	(% 13.8) 4	0.772
	Grade I	7 (38.9%)	5 (45.5%)	12 (41.4%)	
	Grade II	9 (50.0%)	4 (36.4%)	13 (44.8%)	

stable in three (12%); and only in one patient, it got worsened. Of the remaining three patients (12%), the visual function was not measurable in two cases due to death, and in one patient it was not available (►**Table 4**). However, one case with no prior visual defect had experienced severe vision impairments after the surgery; although, the defect showed a marked improvement during follow-up visits.

Pituitary function of the patients before and after surgery is being displayed (►**Table 4**). EES did not improve the hormonal function in any of the cases with prior defects. Even, one of the three patients who had normal pituitary function prior to surgery developed pan-hypopituitarism after EES.

Seventeen (58.6%) patients had diabetes insipidus (DI) before surgery; and in only two (11.7) of the patients, it disappeared. However, out of the 12 patients without prior DI, six (50%) patients experienced DI after surgery as well. In almost half of the patients (48.3%), pituitary stalk was sacrificed because of tumoral involvement. In two patients (6.9%) because of previous surgery, stalk was not detectable. ►**Table 5** demonstrates the frequency of DI and preservation of pituitary stalk in different types of Kassam classification.[12]

As it is shown, the majority of patients had Kassam type II. 71.4% of patients whose pituitary stalk was sacrificed during surgery had DI before surgery, and after surgery all of them had DI (100%).

Follow-Up

The average duration of follow-up was 25 months (3–49 months), during which four (15.3%) patients experienced a relapse. No statistically significant difference was observed between the initial tumor resection rate and the recurrence incidence ($p = 0.103$). Moreover, the tumor size (diameter greater than or less than 5 cm) and the history of previous intervention (primary or secondary) did not affect the recurrence rate as well ($p > 0.05$). Recurrence rates were not different among children or adults ($p > 0.05$; ►**Table 6**).

The median preoperative Karnofsky Performance Status Scale (KPS) of the patients was 90 and it increased to 100 after surgery and during follow-up. KPS increased in all patients who were discharged from hospital after tumor resection.

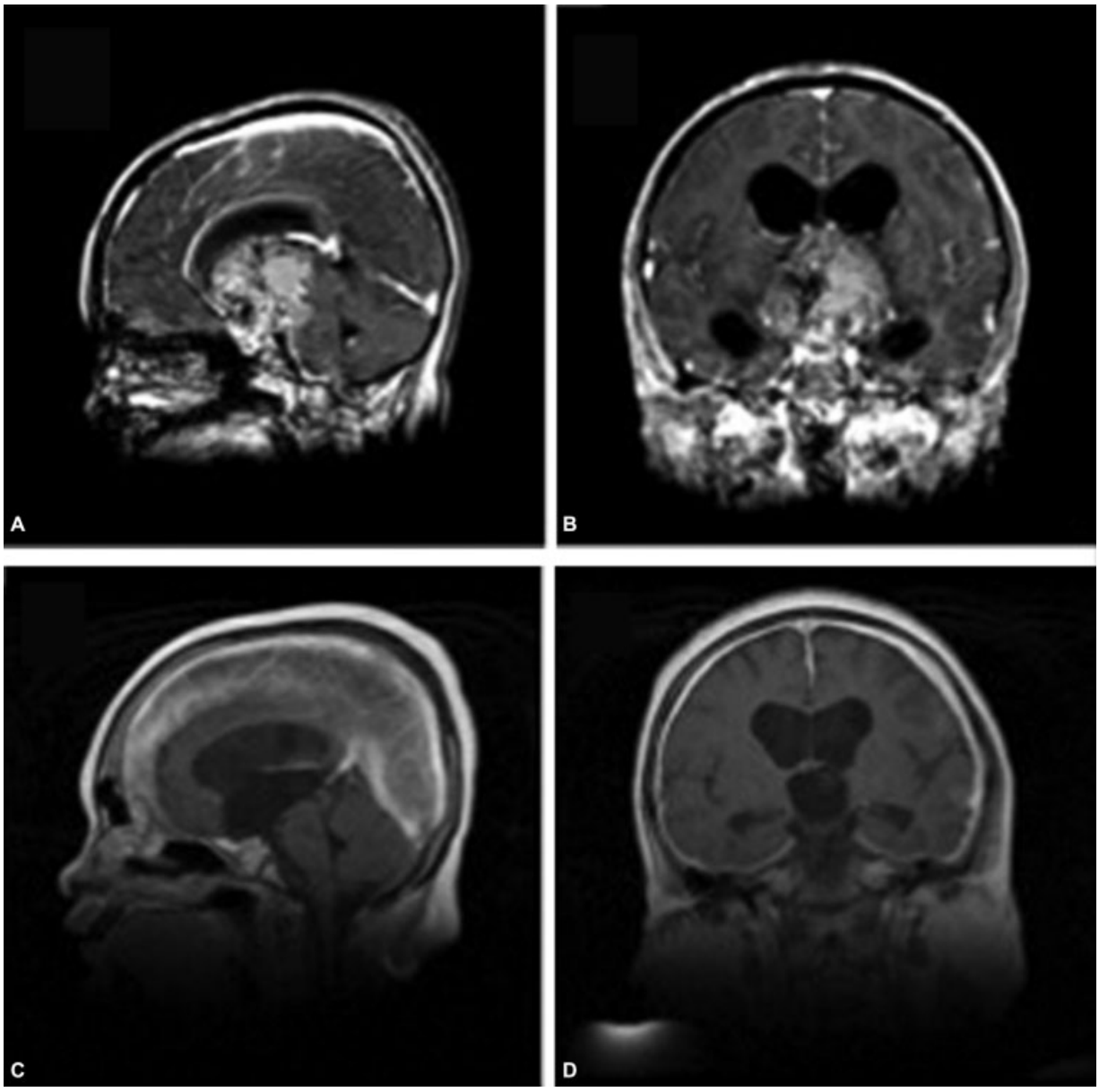

Fig. 1 (**A, B**) Preoperative sagittal and coronal postcontrast T1-weighted MR images in an 11-year-old girl showing a huge calcified tumor extending up to the roof of the third ventricle. (**C, D**) Sagittal and coronal postcontrast T1-weighted MR images obtained 16 months after surgery showing GTR without any recurrence. Patient also underwent a V-P shunt. MR, magnetic resonance.

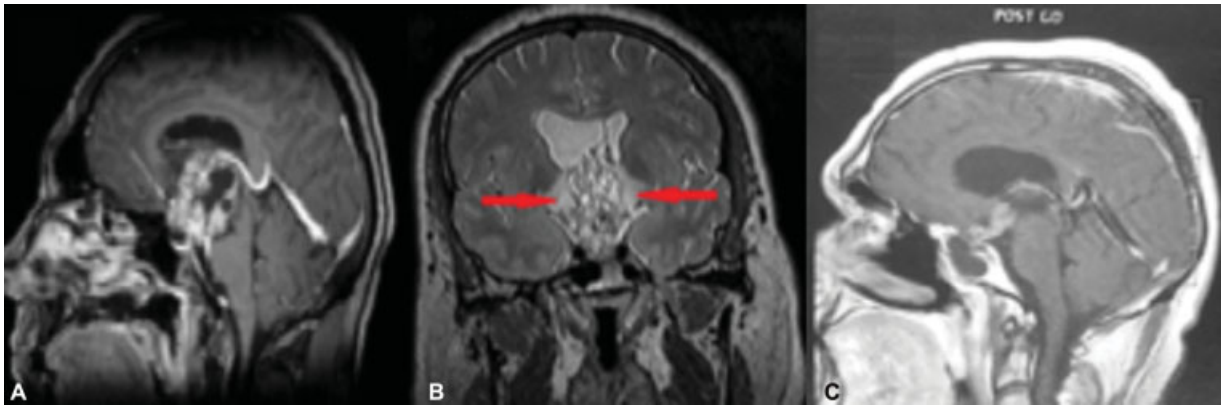

Fig. 2 (**A**) Preoperative sagittal T1-weighted MR image with contrast injection showing a tumor with solid and cystic components. (**B**) Preoperative sagittal T2-weighted MR image denoting a tumor with hypothalamic involvement as Puget grade II (arrowheads). (**C**) Sagittal postcontrast T1-weighted MR image after surgery demonstrating residual tumor because of the severe adherence of tumor to the hypothalamic area. MR, magnetic resonance.

Table 3 Resection rate based on various parameters

Parameter and *p*-Value	Total number	GTR (100%)	Near total resection (>95%)	Resection >95% (GTR + NTR)	Subtotal resection (>80)	Partial resection (<80%)
Total	29	18 (62%)	7 (24.1%)	25 (86.2%)	2 (6.9%)	2 (6.9%)
Primary	18	12 (66.7%)	4 (22.2%)	16 (88.8%)	1 (5.6%)	1 (5.6%)
Secondary	11	6 (54.5%)	3 (27.3%)	9 (81.8%)	1 (9.1%)	1 (9.1%)
p-Value		0.696	0.999	0.622	0.999	0.999
Max. tumor diam. <50 mm	21	13 (61.9%)	4 (19%)	17 (81%)	2 (9.5%)	2 (9.5%)
Max. tumor diam. >50 mm	8	5 (62.5%)	3 (37.5%)	8 (100%)	0 (0.0%)	0 (0.0%)
p-Value		0.999	0.357	0.552	0.999	0.999
Puget grade 0 and I	16	11 (68.8%)	4 (25%)	15 (93.8%)	0 (0.0%)	1 (6.3%)
Puget grade II	13	7 (53.8%)	3 (23.1%)	10 (76.9%)	2 (15.4%)	1 (7.7%)
p-Value		0.466	0.999	0.299	0.192	0.999

Abbreviations: GTR, gross total resection; NTR, near total resection.

Table 4 Visual and hormonal states of patients after EES

Visual/pituitary dysfunction	Total	Improved	Unchanged	Worsened	Nonassessable
Visual field deficit	25 (100%)	18 (72%)	3 (12%)	1 (4%)	3 (12%)
Ant. pituitary dysfunction	26 (100%)	0	15 (57.6%)	8 (30.7%)	3 (11.5%)

Table 5 Frequency of DI and preservation of pituitary stalk in different types of kassam classification

Variable	Kassam type				Total
	I	II	III	IV	
Patients no.	1 (3.8%)	18 (69.2%)	6 (23%)	1 (3.8%)	26
Stalk preservation	1 (100%)	6 (33.3%)	4 (66.7%)	0	(% 42.3) 26/11
Postop. DI	0	14 (77.7%)	3 (50%)		17/24 (70.8%)
Preop. DI	0	13 (72.2%)	0	1 (100%)	14/26 (53.8%)

Abbreviation: DI, diabetes insipidus.

Table 6 Comparison of tumor recurrences with different parameters

Parameter	Total number	Recurrence	*p*-Value
GTR	15		0279
Non-GTR	11		
Resection >95%	22	3 (13.6%)	0.511
Resection <95%	4	1 (25%)	
Adults	19	3 (15.8%)	0.999
Childs	7	1 (14.3%)	
Primary	15	2 (13.3%)	0.999
Secondary	11	2 (18.2%)	
Tumor max. diam. >5 cm	8	2 (25%)	0.661
Tumor max. diam. <5 cm	18	2 (11.1%)	
Total	26	4 (15.3%)	

Abbreviation: GTR, gross total resection.

Complications

Four patients had cerebrospinal fluid (CSF) leakage (rhinorrhea). Three patients experienced CSF leakage in the first week after EES and one patient had this complication after a lapse of 3 months. All of these patients underwent EES for the reconstruction as soon as possible after the leakage event. Two patients experienced *Klebsiella pneumoniae* meningitis, in one it was eradicated by antibiotic treatment, and subsequently VP shunt was placed due to evolving of hydrocephalus; unfortunately, the other patient died due to the meningitis resistant to the antibiotic regimen. Finally, one death in a well conscious 2.5-year-old girl occurred due to aspiration at midnight 3 days after surgery.

Discussion

Given the previously performed studies, surgical resection seems to be the ideal modality for craniopharyngiomas. However, GTR is not always achievable due to different tumors' consistency, size, and adhesions to the vital neurovascular

elements. Transcranial approaches, due to their extensions and limitations, may be associated with several complications like visual or vascular damages. On the other hand, the EES approach provides proper visual and physical access to the pituitary stalk and infundibulum, the floor of the third ventricle, and the hypothalamus. Furthermore, the GTR in the EES approach is greater or at least the same as transcranial approaches and shown to be associated with less complications.[13,14] Beside all of these findings, the transcranial approach has remained as the best route for intraventricular tumors and tumors with lateral extensions.[15] In the cases with vital organs involvement, the surgeon's experience is another important factor.[16] Although the present study consists of small number of patients, it adequately demonstrates the role of EES in the treatment of craniopharyngioma.

Different studies have reported a GTR of 29 to 90% for craniopharyngioma (►**Table 7**). In this regard, the results of the current study show the rate of GTR for the primary and recurrent/residual craniopharyngiomas as 66 and 54.5%, respectively. In general, out of 29 patients, 25 (86.2%) experienced a resection of over 95% which was indeed significant. In another similar study performed by Bal et al[7] on 25 patients with craniopharyngioma, GTR was 76% in patients with recurrent and 87% in primary cases. The study of Cavallo et al[17] is one of the studies with a large number of craniopharyngioma cases. In their retrospective study, evaluating EES results in 103 patients with craniopharyngioma from 1997 to 2012, it was shown that the GTR was achieved in 68.9% of the cases. However, in patients with a prior history of surgery, it was 62.1%. In the study of Koutourousiou et al,[11] GTR rate was 37.5% in 64 cases with craniopharyngioma as well as the NTR rate (>95%) in 34.2% of the patients. In this study, when the tumor capsule could not be detached from adjacent vital neurovascular structures, NTR instead of GTR, and postoperative radiotherapy was preferred. Although the management of craniopharyngioma remains somewhat controversial, numerous studies have demonstrated that, STR with adjuvant radiotherapy has similar therapeutic value as GTR.[18–20] After all, if safe resection is possible, GTR as the initial treatment should be attempted to reduce the tumor recurrence. However, if the tumor recurs after the first surgery, radiotherapy or gamma knife radiosurgery with/without reoperation may be an effective salvage treatment for recurrent craniopharyngioma.[21]

Previous studies have indicated that transcranial surgeries have been associated with more visual complications compared with microscopic transsphenoidal surgery (TSS) and EES.[14,22,23] Endoscopic approach provides a panoramic view, remarkably visualizing the tumors' margins. This enhances separating the tumor from surfaces and vital elements like the chiasm and optic nerves, and the hypothalamic area. Using EES, the chance of physical trauma and vascular damage caused by the blind dissection of the opposite side of the tumor would significantly decrease.[23,24] In this regard, the study by Chakrabarti et al on the 86 patients with craniopharyngioma, revealed that the visual function was improved only in 61% of the patients who had undergone transcranial surgery, while in the TSS group, the improvement rate was as high as 87%.[25] In the present study, most patients (92.3%) had stable or improved visual function after EES, and only two (7.7%) patients experienced new visual impairment which conforms to previous studies. These findings are in accordance with previous studies showing that patients with craniopharyngioma who were

Table 7 Previous endoscopic endonasal surgery series for craniopharyngioma and this study

Reference	No.	GTR (%)	Follow-up (mo)	Vision improvement (%)	New DI (%)	New HP (%)	Meningitis (%)	CSF leak (%)	Recurrence (%)	Perioperative mortality (%)
Gardner et al 2008[26]	16	73	34	93	8	18	0	58	25	0
Jane et al 2010[10]	12	42	13	78	44	67	8.3	0	–	–
Campbell et al 2010[32]	14	29	–	86	7	57	14.2	36	7	0
Leng et al 2012[34]	26	86	35	77	42	38	4	3.8	25	0
Koutourousiou et al 2013[11]	64	37.5	38	86	47	58	7.8	23	34.4	0
Bosnjak et al 2013[8]	8	75	27	75	62	62	25	25	–	–
Cavallo et al 2014[17]	103	75	48	75	48	46	1	14.6	22.3	1.9
Yadav et al 2015[36]	44	59	19	77	14	9	2.2	9	13.6	2.2
Fomichev et al 2016[25]	136	72	42	52	42	42	16	8.8	20	5.8
Bal et al 2016[7]	25	80	56	94	50	80	0	12	–	0
Park et al 2017[37]	116	46	35	76.4	25.5	47.4	6	11.2	15.5	0
Dho et al 2018[38]	68	91.1	48	64.7	52.4	47	1.4	2.9	2.9	0
Our series	29	62	25	72	50	34.6	6.9	13.8	15.3	6.9

Abbreviations: CSF, cerebrospinal fluid; DI, diabetes insipidus; GTR, gross total resection; HP, hypopituitarism.

treated with EES approach had a visual improvement of more than 70% (►**Table 7**).[17,26]

The overall incidence of new endocrinopathy in transcranial craniopharyngioma surgeries is 37% and varies from 20 to 80% in series with EES approach (►**Table 7**). In the current study, we observed new pituitary hormonal dysfunction in 34.6% of our patients with no improvement. Hormonal status did not change in 65.4% of the patients. The same results were obtained by Fomichev et al.[25] In their study in Russia on 136 patients with craniopharyngioma, hormonal improvement was not observed in any of the patients and the rate of hormonal worsening was 42.6%, which is 6% higher than that of our study. In our study, the occurrence of new DI despite the preservation of pituitary stalk could be due to various reasons including tractional trauma to the stalk and its internal vessels, the hypophyseal artery, or vascular spasm.

Craniopharyngioma tends to recur even after GTR. In studies with significant number of samples,[27,28] the recurrence rate in patients who had undergone GTR has been reported between 0 and 53%, and between 30 and 100% in patients with subtotal or partial resection. In the study by Koutourousiou et al,[11] the recurrence rate was 25% in patients with GTR and 34.4% in all patients. In our survey, these rates have been shown as 6.7 and 15.3%, respectively with a shorter follow-up period. Furthermore, it has been shown that in transsphenoidal endoscopic surgery, the recurrence rate is between 7 to 34%, as shown (►**Table 7**). It seems that one of the most important factors affecting the recurrence is the resection rate during the initial surgery.[29] Moreover, the large size of the tumor (diameter of above 5 cm) has been observed to be associated with greater recurrence rate[30]; however, in our study, no significant difference was seen in the relapse rate among patients with different amount of the tumor resections or different tumor sizes, which is probably because of the low number of patients and the recurring cases. Radiotherapy is the main adjuvant therapy after EES, which is used as a surgical supplement in cases where the tumor residue is significant.[18,30] In our study, from the five patients with residue after the surgery, four patients underwent radiotherapy.

CSF leakage (rhinorrhea) is one of the most common and challenging complications after TSS (whether microscopic or endoscopic). Maira et al[31] who had used TSS for craniopharyngioma, reported a leakage rate of 17.5%. In endoscopic studies like the study by Campbell et al,[32] this rate was reported as 36%. In 2007 and 2016, Divitiis et al and Fomichev et al[25,33] conducted two studies on patients with craniopharyngioma by extended transsphenoidal endoscopic approach, with a CSF leak rate of 20 and 8.8%, respectively. In our study, CSF leakage rate was 13.8%. Pedicled nasoseptal flaps can significantly decrease CSF leakage rates. In this regard, the recent studies by Jane et al[10] and Leng et al[34] have shown incidence rates of 0 and 3.8%, respectively.

The incidence of meningitis has been reported as 0 to 25% while postoperative hydrocephalus had an incidence rate of 0 to 21.4% in endoscopic endonasal approach[27,31,32] (►**Table 7**). Two of our 29 patients (6.9%) experienced meningitis, one of whom had EVD and the other had a CSF leakage after surgery.

In the study by Fomichev et al,[25] the mortality rate was 5.8% (six patients). It occurred in one patient due to bacterial meningitis, in two patients due to myocardial infarction and pneumonia, and in the three other patients due to hemorrhagic complications associated with intraoperative injury of large arterial vessels or delayed bleeding in the postoperative period. In the study by Cavallo et al,[17] perioperative motility has been reported in two cases out of 103 patients (1.9%). In this study, the perioperative mortality (death during the first 30 days after surgery) was seen in two patients (6.9%). In one case, the cause was meningitis and intraventricular hemorrhage, and in the other case, who was a 2.5-year-old child, the death was due to midnight severe aspiration; this event emphasizes that the early postoperative period in a young child with tamponade noses is very critical and needs more precise care than adults.

The main limitation of this study was the small number of the included patients and thus the subgroups, such as the children or the patients with recurrent tumor; hence, proper comparisons were not achievable in some cases. In addition, the follow-up periods were rather short, and in general, a longer follow-up duration was needed to interpret the surgical results more accurately.

In conclusion, the results of the current and previous similar studies show that the resection of suprasellar and intrasellar craniopharyngiomas with endoscopic endonasal approach is an effective and less-traumatic method with low postoperative complications, as well as low mortality rates. Safe GTR is the goal of surgery; however, in those cases where GTR might be associated with high risks, NTR (above 95%) or STR should be considered. In addition, the EES results are acceptable and comparable to transcranial approaches.[14,22,23] Besides these findings, transcranial approach remains an acceptable route for intraventricular tumors and tumors with considerable lateral extensions.[16,23] In intrasellar/infradiaphragmatic or supradiaphragmatic–infrachiasmatic lesions, EES could be the best alternative for surgery, but in suprachiasmatic–retrochiasmatic lesions the transcranial approach could be a better alternative.[35] In our study, the EES approach has been associated with high rates of visual improvement and GTR, and also found to be suitable for recurrent cases.

Conflict of Interest
None declared.

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